Intrathecal Medication Administration in Cerebral Palsy

43

Julieanne P. Sees and Freeman Miller

Contents

Abstract

Administering medication directly into the intrathecal space, especially in the spinal canal, has continued to be of interest. A drug concentrated in this region of the nervous system should provide the most direct effect. The current administration of intrathecal baclofen has been used for this reason by means of a battery powered pump implant that is placed in the abdomen and an intrathecal catheter that is introduced into the intrathecal space within the spine. The pump is controlled with an external radiowave-mediated controller, and the pump reservoir is filled by direct injection through the overlying skin. The administration may be continuous or the pump can be programmed to have higher doses over a short time and utilize a flexible dosing regimen as desired. Rare potential side effects have been reported including infection, catheter malfunction, and weakness uncovered with reduction in spasticity. The treatment of intrathecal infusion of baclofen is widely beneficial in the management of movement disorders, severe spasticity, enhancement of range of motion, increase in motor function and mobility, alleviating discomfort, and aids in overall care whether used stand alone and/or in conjunction with common modalities of pharmacology agents, physical therapy, and orthopedic surgery for nonambulatory and ambulatory patients with cerebral palsy.

Keywords

Intrathecal baclofen pump · ITB · Intrathecal medication administration · Antispasticity medication · Movement disorder management

J. P. Sees (✉)
Nemours Alfred I. DuPont Hospital for Children, Wilmington, DE, USA
e-mail: JSees@nemours.org; julieanne.sees@nemours.org

F. Miller
Department of Orthopaedics, Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE, USA
e-mail: freeman.miller@gmail.com

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Introduction

Over the past 30 years, the significance in administering medication directly into the intrathecal space, especially in the spinal canal, has continued to be of remarkable interest and development. Since there is a general perception that spasticity originates in the spinal segments, a high dose of drug concentrated in this region of the nervous system should be given to provide effect. This route was initially developed to administer morphine (Erickson et al. 1985) but has quickly been applied to administration of baclofen (Zierski et al. 1988). The intrathecal pump is a battery powered implant which is placed in the abdomen, and an intrathecal catheter is introduced into the intrathecal space within the spine. This catheter is tunneled subcutaneously around the lateral side of the trunk to the anteriorly implanted pump site and connected to the pump. The pump is controlled with an external radiowave-mediated controller, and the pump reservoir is filled by direct injection through the overlying skin (Case 1). The primary medication used to manage spasticity by intrathecal pump administration is baclofen. The administration may be continuous, or the pump can be programmed to have higher doses over a short time, then greatly reduced for a period of time, and thus utilize a flexible dosing regimen as desired.

Natural History

The use of intrathecal administration of baclofen was first approved by the FDA for use in children in 1997. At the time of approval, there were fewer than 200 children with implanted pumps. In the past 20 years, these pumps have become much more common. These pumps have the tremendous advantage of being adjustable and can be discontinued at any time should the results not be thought of worth the trouble. Usually in an initial consultation, the clinician makes a careful assessment with a listing of the caretakers' concerns. If the child has not had a spinal fusion, a trial dose may be performed with 75–100 mg injected as a bolus dose in the epidural space. At our institution, typically trials are not necessary on all patients, but for the ambulatory patients, this is strongly recommended and performed often with concurrent gait laboratory analysis to assist in the decision-making process. Caretakers and the medical team then monitor the child and a joint decision is made as to the benefits. For especially difficult cases, an indwelling catheter, which can be left in place for several days, may be used so the dose can be adjusted. This implanted catheter is used for children with greatly variable tone, or individuals in whom adjustable doses of baclofen are to be monitored.

Treatment

The initial recommendation was to do a series of three injections on consecutive days starting with 25 mg, then 50 mg, and then 100 mg on the third day (Albright et al. 1991). We have not found this algorithm very useful and prefer to give a single dose of 75–100 mg via the inserted catheter (Albright et al. 1996). Children either do or do not respond, and the small dose differences in the prior recommendation add little to understanding the effect. Also, the recommendation that children be tried on oral baclofen (Albright et al. 1991) has little merit, as there are no data suggesting that it is helpful in children with CP. Our experience has been that oral baclofen is almost never of any beneficial predictive value. As suggested in the "Best Practices for Intrathecal Baclofen Therapy: Screening Test (Boster et al. 2016)," the algorithm our colleagues and we use for intrathecal baclofen is to do a clinical evaluation, if warranted followed by one injection trial, then the pump delivery system is implanted surgically and adjustment of the dose is done on bi-monthly basis until maximized therapeutically to the child's needs. We infrequently use the small 20-ml pump because it is only minimally smaller than the 40-ml pump but has a capacity that is almost 50% less. This capacity becomes very significant when the child requires a high dose of baclofen, such as 1000 mg per day. If the 20-ml pump is used, it must be filled much more frequently even if the 2000 mg/ml concentration for

baclofen is used. This type of dose is not uncommon, and the size of the child is not related to their baclofen needs.

Case 1: 8 Year Old Girl

Here is an 8-year-old girl who is mentally challenged with severe spastic quadriplegia. She is completely dependent for all care needs. Her mother's complaint is that she has difficulty with diapering, dressing, and bathing. Sometimes the child would have severe extensor posturing which made seating rather difficult. She would sleep well, fed by gastrostomy tube, and has seizures several times a day, which were felt to be well controlled, and weighed 16.7 kg. A pump was inserted with good spasticity relief (Figs. 1 and 2). Over 6 months, she continued to have rapid accommodation to the drug; however, a plateau dose of 650 μg was reached that continued to control her spasticity. She had little body fat with the pump visible with slight prominence on her abdomen (Figs. 3 and 4).

The outcome of administering baclofen via intrathecal pump is a clear reduction in spasticity in most children. After the initial implantation, it may take 3–6 months before a constant level of drug that will keep the spasticity decreased is found. The drug accommodation effect is well known in the oral use of baclofen and occurs with intrathecal dosing as well. However, when a certain optimal dose is reached, this accommodation effect no longer occurs. The required dosing for individual children varies greatly and is not related to body size. The dose requirements vary from 100 mg to 2000 mg per day. The correct dosing can be determined only by slowly increasing the dose and evaluating the effect on the child. After spasticity reduction has been accomplished, the functional gains are extremely variable, with the clearest gains occurring in children with quadriplegic pattern involvement

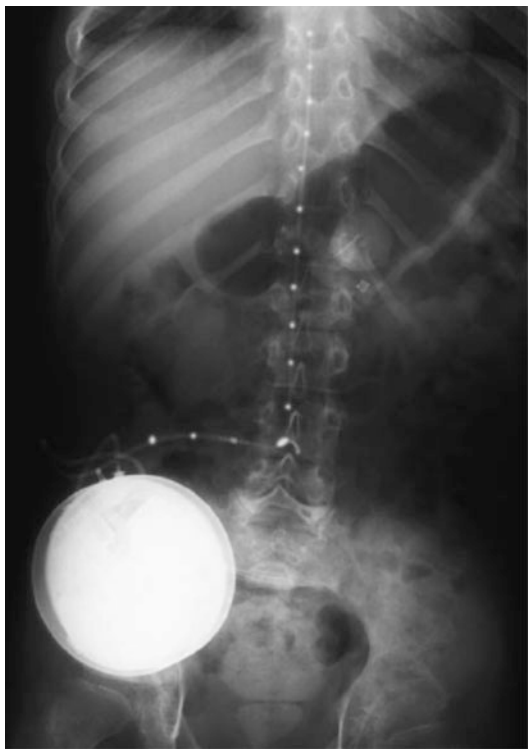

Fig. 1 Pump inserted with good spasticity relief

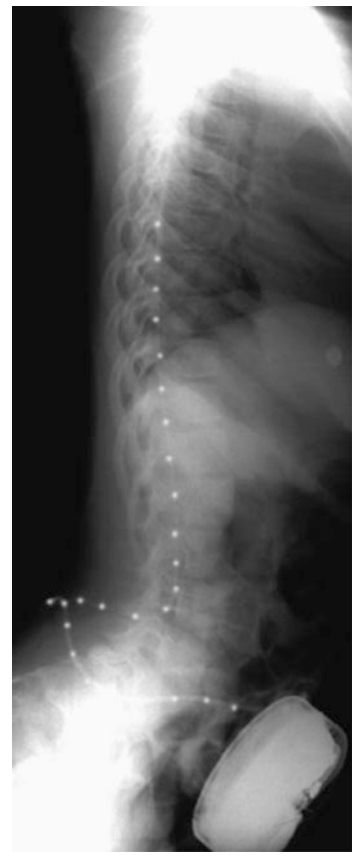

Fig. 2 Pump inserted with good spasticity relief

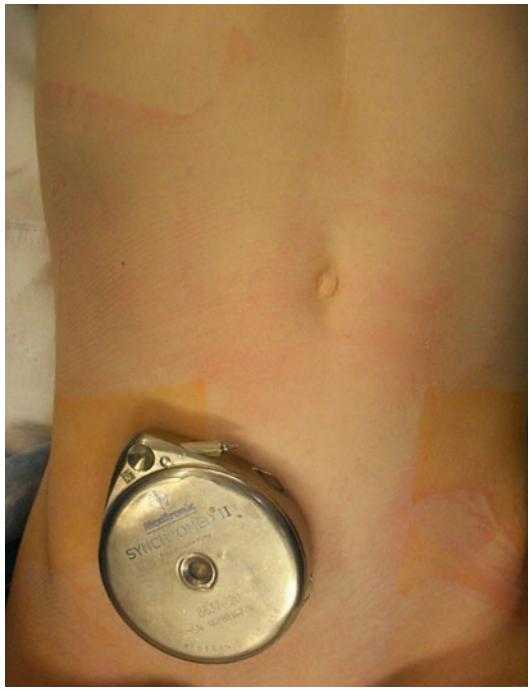

Fig. 3 The baclofen pump placed externally in the location where bit will be implanted in the right lower quadrant of the abdomen

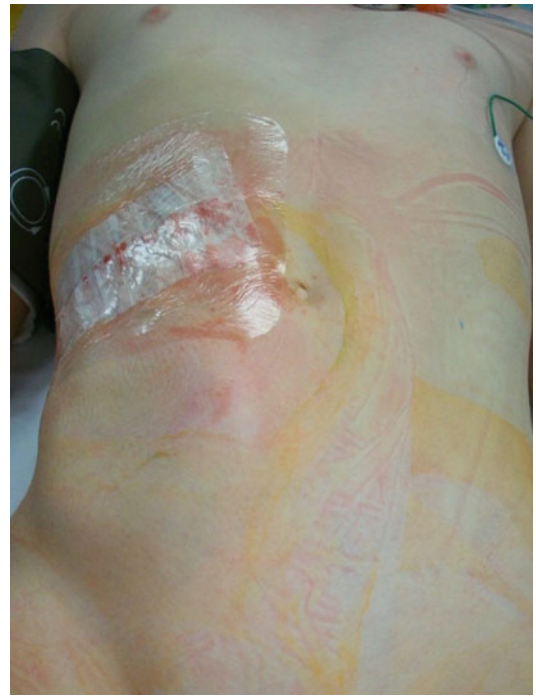

Fig. 4 Pump visible with slight prominence on abdomen

based on subjective reports from caretakers. These caretakers report improved ease of dressing and other activities of daily living (Albright 1996a; Almeida et al. 1997). Improved sleeping has been noted in many of our patients, as well as behavior improvements. Improved sitting and upper extremity use are also reported quite often by the families (Armstrong et al. 1997; Albright 1996b). All these functional gains are subjective reports that usually make the families very happy with the device. The use of intrathecal administration of baclofen in ambulatory children has very minimal experience and is used mostly in older children with severe gait disturbances (Albright 1996b; Gerszten et al. 1997). Attention must be given particularly to those patients where a decrease in tone may lead to a decrease in ambulatory function. We found in our study of ambulatory children that some gait kinematic improvements such as knee flexion at initial contact was helpful to gait; however, it can be difficult to determine whether reduced tone is improving function or uncovering underlying weakness. Namely, in our study, three adolescents, one GMFCS II and two GMFCS III, preferred more spasticity because it provided a sense of stability and strength to them, assisting in their ambulatory ability (Pruszczynski et al. 2017). Our experience, as well as the experience reported to us from other gait laboratories, suggests that children's speed does not change, but there may be some increased range of motion at the knee to enhance potential for strengthening in gait while in some children the tone reduction instead may lead to further crouch. Uncovering an underlying component of weakness especially during the adolescent growth period can confound the pump benefit.

Complications

Complications with the use of the intrathecal pump vary; however, the rates are worth mentioning. Incidence of infection in the literature has been reported anywhere from 0% to 25% (Albright 1996a; Armstrong et al. 1997; Wiens 1998). In our experience, infection of the pump

system is 2.4% per procedure, while the risk of late infection over 5-years was 0.95% per year (Bayham et al. 2016). Mechanical catheter problems have been reported as well, including catheter breakage, disconnections, and kinking (Zierski et al. 1988; Albright 1996a; Armstrong et al. 1997). Pump pocket effusion and persistent cerebrospinal fluid (CSF) leakage have also been reported (Almeida et al. 1997). The acute withdrawal of baclofen, if it is given either intrathecally or orally, may cause children to have hallucinations and acute psychosis (Kita and Goodkin 2000). The complications of the baclofen pump are generally easy to treat and do not have permanent consequences. Most infections that involve the pump require that the pump be removed and the infection cleared; then the pump can be reinserted. We have been able to treat initial pump pocket infections during the same surgical setting insertion by placing a new pump at a different anatomical site from the infected pump pocket. (Fig. 5) The new fresh pump is then connected to the old catheter at a site removed from the infection site. This approach with removing of the infected pump has been successful when the infection is localized to the pump pocket and the patient is not septic. Most infections of the spinal catheter are treated with removal of the catheter and upon subsequent infection clearing, then reinsertion of the catheter. We also have treated one patient who presented with a ventriculoperitoneal (VP) shunt infection with a course of intravenous antibiotics and acute intrathecal catheter exchange with no complications, and there is one report in the literature where intrathecal vancomycin hydrochloride was used in the pump and the pump was saved (Bennett et al. 1994). In our series of 313 children managed with intrathecal baclofen therapy, 31 children had VP shunts, with two patients having infection of both systems and three patients had infection in one system (Abousamra et al. 2017). Our recommendation suggests if aspiration from both systems shows positive cultures, treatment should be removal of both systems, while if the primary system does not show positive cultures, it may not need removal but close follow-up is strongly encouraged with a high level of suspicion for any sign of infection or malfunction.

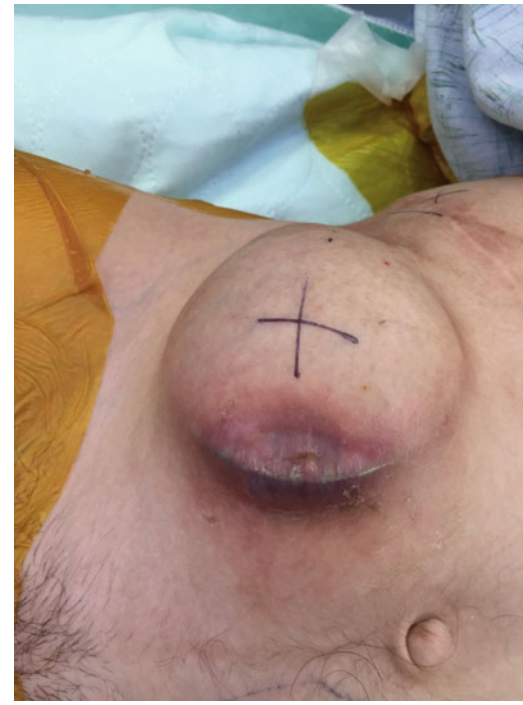

Fig. 5 A child with a pump pocket infection who was treated with removal and reimplantation of new baclofen pump at different anatomical site

An important technical detail that will avoid wound problems over the pump in thin children is to make sure the incision used to insert the pump is very proximal so none of the scar resides over the pump or catheter after implantation. This means that the incision to insert the pump may be at the level of the lower ribs. All wound problems we have encountered have been in cases where the incision ended crossing the underlying pump, usually at the junction where the catheter inserts into the pump (Fig. 6). Inserting the pump under the external oblique fascia is another option that will help with soft-tissue coverage. The major problem with catheter complications is diagnosing the problem. Sometimes children are not responding as expected, or suddenly stop responding, to the baclofen. If this occurs, there may be a possible catheter problem. The first study should be a radiograph to evaluate the catheter. Sometimes the radiograph will be able

to visualize catheter discontinuity (Fig. 7). An attempt in the clinic can be made to aspirate from the catheter aspiration portal which may itself demonstrate discontinuity with a dry tap. Injection with a radiopaque material may also be used followed by a radiograph or as we have developed a protocol using the computed tomography study for a safe and an effective modality in locating defects along the intrathecal baclofen delivery system with ultimately having advantage to guide surgical specific solutions (Abousamra et al. 2016). Normal CT findings with the injected material flowing freely through the catheter are depicted on axial cuts as a perfectly layering fluid which forms a crescent shape around the catheter tip in Figs. 8 and 9 and the fluid gradually dilutes as the cuts proceed in the caudal direction. Inadequate contrast pooling can be noticed on the CT scan as in Figs. 10 and 11 where the fluid distribution layers lose the crescent shape. Areas of leakage such as fluid collection around the pump (Fig. 12), along the catheter (Fig. 13), or sequestration at the catheter tip (Fig. 14) are easily evident with CT scan evaluation. If this study is inconclusive, there is a serious concern; the child should be taken back to the operating room and methodically investigated where the anterior catheter pump connection is exposed, the catheter is removed, and there should now be the ability to obtain CSF from the catheter. If not, the posterior catheter has to be exposed, disconnected, and whichever section is not patent should be replaced.

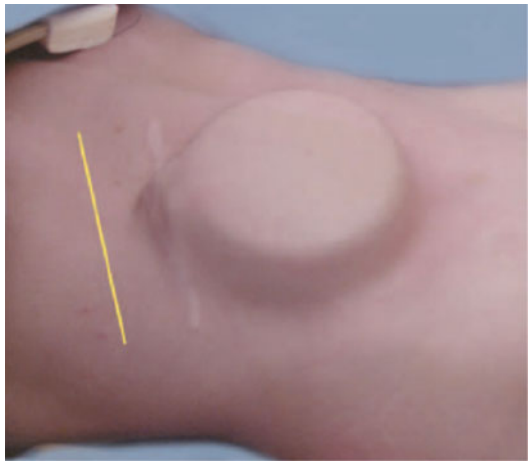

Fig. 6 The incision for the baclofen pump should be higher than the expected placement site of the pump. This is to prevent the incision from being directly across the connectors of the pump, as shown in this picture, since there is a higher risk of wound breakdown and possible complication. Ideally the incision should be well away from the pump pocket, as shown by the *yellow line*

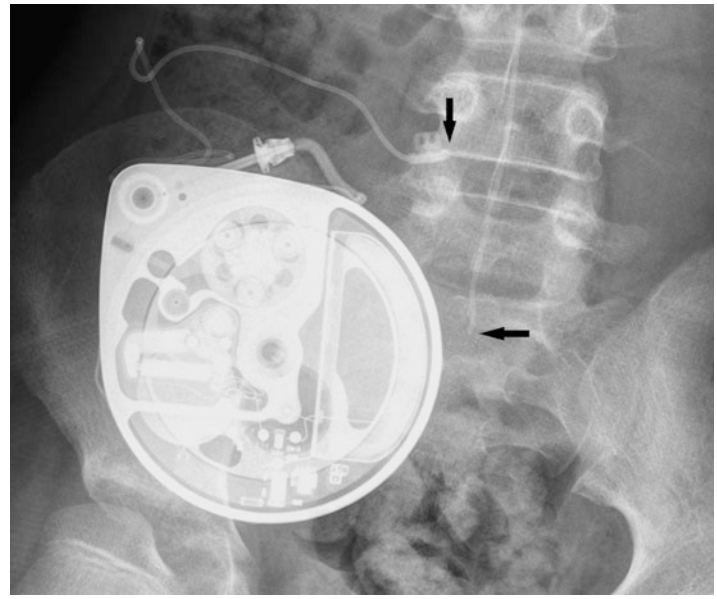

Fig. 7 A plain radiograph showing a catheter fracture with the two ends of the fracture (arrows)

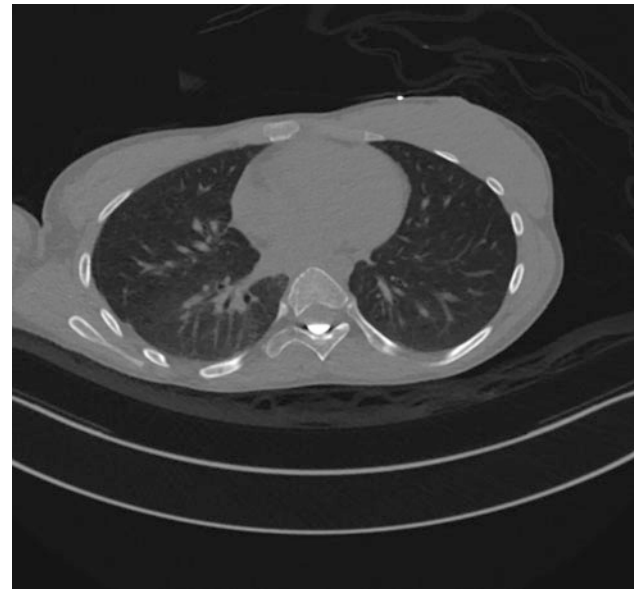

Fig. 8 Normal CT scan with the contrast medium forming a perfect crescent free from the catheter

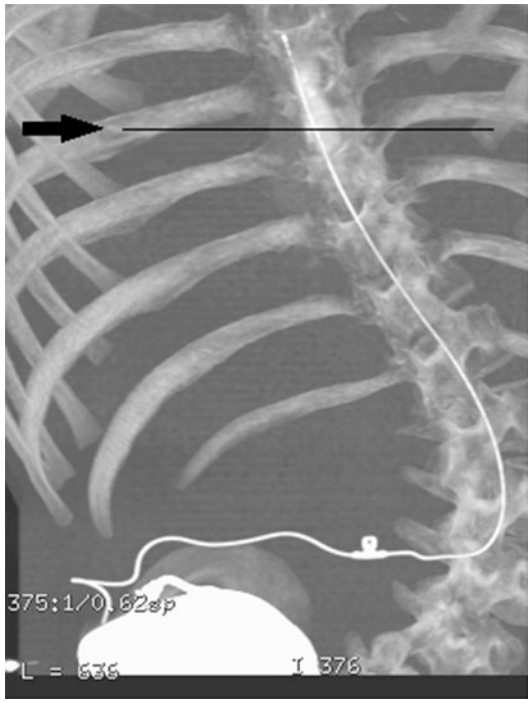

Fig. 9 Three dimensional CT reconstruction of the same patient in Fig. 6 with the cut level shown (arrow). The whole catheter length can be tracked on this type of imaging

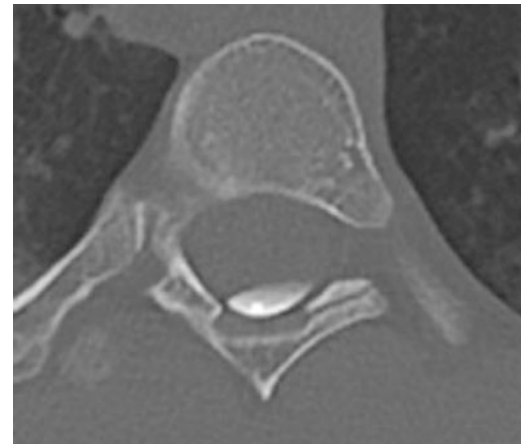

Fig. 10 Inadequate pooling of the contrast. The fluid fails to form the crescent shape and it does not flow free from the catheter

Another complication that may occur is in a child who maintains a CSF leak after insertion of the catheter. The initial treatment is to leave the child in a supine position for up to 2 weeks to see if this leak resolves. The primary symptom from this CSF leak is a severe headache and nausea. In most cases, with time the leak stops, and to assist if swelling is visible at the spinal incision, a pressure dressing with abdominal binder may also be used. We have had children who continued to leak despite conservative measures. One child had a posterior spinal fusion in which the fusion mass had been opened. This wound again was opened, and the fascia was placed over the dura

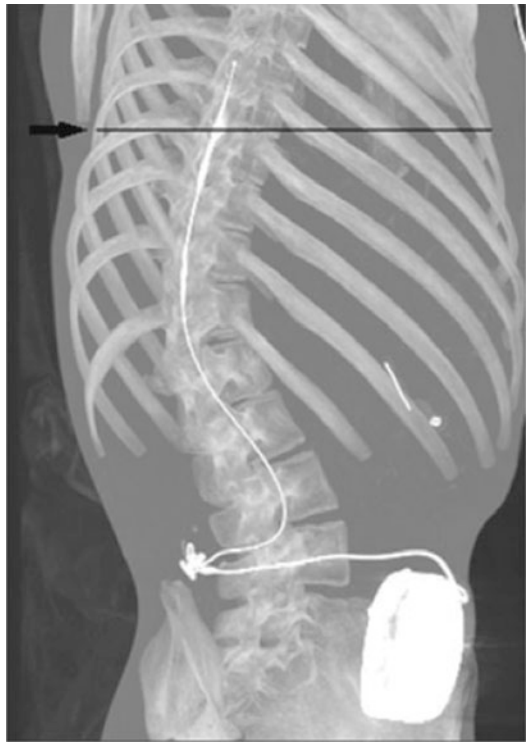

Fig. 11 Three dimensional CT reconstructions with the cut level of Fig. 8 shown (arrow)

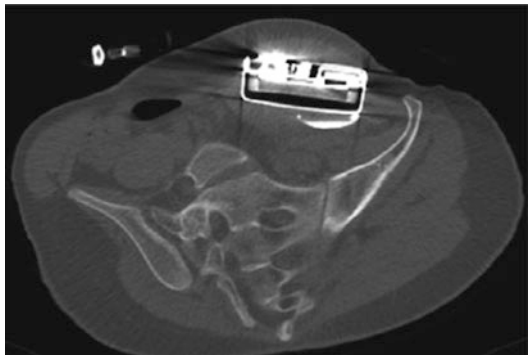

Fig. 12 Fluid collection around the pump indicates a leak at the pump catheter connector

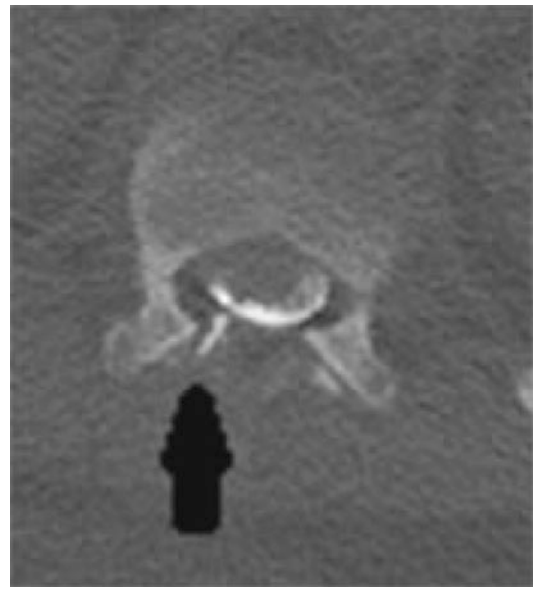

Fig. 13 Fluid seen in the lumbar spinal canal at and below the catheter level (arrow) indicative of a leak just before the catheter enters the canal

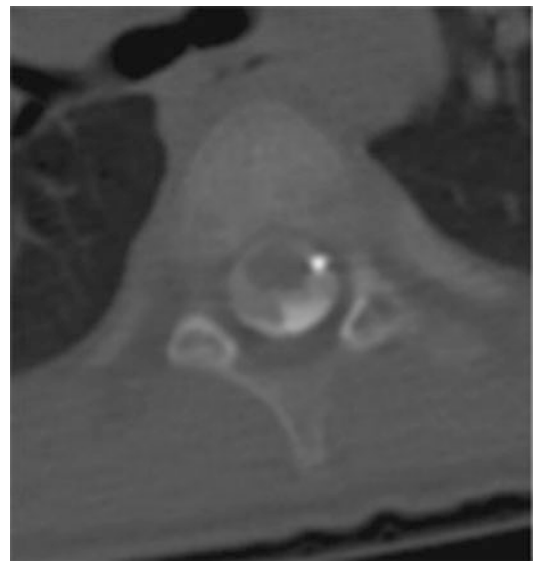

Fig. 14 Fluid sequestration seen around the catheter tip

with closure of the bone defect with methyl methacrylate. If an opening in the fusion mass is done to insert the catheter, the bone defect is now routinely closed with a Tisseel Fibrin or hemostatic matrix sealant. If the child has not had a spinal fusion, an epidural blood patch may be tried. This patch works well if a leak occurs following a trial injection, and, in some cases, in stopping leaks around inserted catheters. In this situation, the insertion site may also need to be exposed and the catheter insertion site covered with a fascial patch.

If there is a sudden malfunction of the implanted pump, it will stop functioning instead of pumping too much. This safety feature of the pump has not been reported to fail. In this circumstance, if there is a question of pump function, the pump needs to be replaced. The battery that powers the pump has an implanted life of approximately 7 years. When the battery loses power, the whole pump has to be replaced. The catheter does not need to be replaced. We recently have observed when vagal nerve stimulator magnets are placed close to the pump pocket the pump has been observed to stall and restart inconsistently. If there is any question as to whether a child's pump is functioning or there is a catheter malfunction, the child should be placed on oral baclofen to prevent the withdrawal psychosis that occurs in some children with appropriate assessment performed. Baclofen also has an antihypertensive effect (Sweet et al. 1979); however, this is seldom a significant problem. There may be a sympathetic blockade-type effect decreasing the overreacting peripheral basal motor response that creates blue feet when the feet get cold (Rode et al. 1999). This is a normal response also seen in adolescent and older individuals who are nonambulatory.

Another well-documented effect of baclofen in rats is a decrease in the number and frequency of penile erections (Agmo and Paredes 1985; Leipheimer and Sachs 1988). There is one report involving adult males with spinal cord injury-induced spasticity treated with intrathecal baclofen. In this report, a significant number of men reported a decreased time and rigidity of erections, and two men reported losing the ability to ejaculate (Denys et al. 1998). One of our patients was a young man whose main complaint with intrathecal baclofen was a decreased quality of his erection and a prolonged latency period between erections. This complication should be mentioned to patients for whom it might be a concern.

A small group of children require a very high dose of intrathecal baclofen, sometimes 2000–3000 mg per day. Also, some children who are on a lower dose suddenly need increased doses if their spasticity is increasing 6 months to 2 years after the implantation. An organized approach must be in place to help optimize intrathecal baclofen therapy and provide troubleshooting in cases of under dose and overdose. Evaluation includes a targeted history of onset, duration, course, physical examination, radiographic/imaging testing, and pump interrogation (Saulino et al. 2016). In cases of somnolence or autonomic instability, children may need more emergent care with hospitalization. If a child has had an increasing need for baclofen, or is requiring a sudden increase in baclofen after having been stable, catheter malfunction should be considered. After the full workup for catheter malfunction, or after demonstration that the catheter is functioning, another option for dosing is to use a drug holiday. In this treatment, the intrathecal baclofen is reduced and then slowly decreased to zero to avoid a withdrawal psychosis. The pump may be left in the turned-off position for 1 month and then the drug slowly reintroduced. This drug holiday should allow the nervous system to redevelop sensitivity to the drug. Another way to use this concept of a drug holiday is to give large intrathecal boluses several times a day instead of continuous dosing. Therefore, instead of giving a continuous dosing rate of 2000 mg, the child may be given 1000 mg just before bedtime, and then another 1000 mg over a 30-min period the first thing in the morning. These different dosing regimens may provide a better benefit in some children compared with continuous administration.

The current role of intrathecal baclofen in the treatment of children with severe spasticity is primarily in nonambulatory children. From a theoretical standpoint, this treatment should also be ideal for the 3–8-year-old spastic ambulatory child for whom a rhizotomy could be considered. The size of the pump and the need for long-term maintenance, with filling at least every 3–6 months, has made it sometimes challenging to convince parents and physicians that this is a good treatment option. Also, there are no objective published data to guide recommendations for the best modality of tone management. This question would be

an excellent project for a well-controlled study similar to the randomized rhizotomy studies (Steinbok et al. 1997; McLaughlin et al. 1998). We do have insight with one investigation of the long-term results of intrathecal baclofen therapy for children with spastic cerebral palsy where there was an improvement in quality of life in children and participants would recommend this mode of treatment and choose baclofen therapy again if given the choice (Kraus et al. 2017). However, there is no good objective data to make recommendations as to the long-term benefit of spasticity management.

Another problem with the current pump is that it has very poor design features, such as having a very superficial catheter connection site, making it a site for skin pressure, and the pump is much more bulky than is really necessary. As better engineered pumps are designed and medication that has more stability is found, it would be better if the pump only needed to be filled every 6 months to 1 year, where it would become an even better option, especially for high-functioning children. Also, there are other medications that may be even better choices than baclofen; however, each of these needs to be trialed and tested in children with spasticity. Despite the shortcomings and less than ideal dilemmas presented by intrathecal baclofen therapy, there have been recent reports in support of its usage from a cost-effectiveness standpoint. Two separate studies demonstrated this, where the first evaluated the net result of the baclofen therapy where it was found to have an incremental cost-effectiveness ratio of $42,000 per quality-adjusted life-year, noting that this is a figure within the $50,000–100,000 range that is widely accepted as offering good value for the money (De Lissovoy et al. 2007). A second study reviewed intrathecal therapy with regards to the life-long costs including if a patient did not have a pump, but would rather have more therapies, office visits, and frequency in additional supportive measures. It found there was a significant reduction in cumulative future medical costs compared to anticipated costs in the absence of a pump implant (Saulino et al. 2015). With both of these studies, as previously noted in the literature, the successful cost effectiveness of the intrathecal baclofen delivery system does provide our only adjustable tone management tool improving the quality of life for children with cerebral palsy.

Cross-References

- ▶ Dorsal Rhizotomy for Spasticity Management in Cerebral Palsy
- ▶ Focal Management of Spasticity in Cerebral Palsy
- ▶ Intrathecal Baclofen Therapy: Assessment and Medical Management
- ▶ Medical Management of Spasticity in Children with Cerebral Palsy

References

Abousamra O, Rogers KJ, McManus M, Miller F, Sees JP (2016) Evaluation of intrathecal baclofen delivery system malfunction by computed tomography scan. Dev Med Child Neurol 58:409–415

Abousamra O, Duque Oroszo MdP, Rogers KJ, Miller F, Sees JP (2017) Infections of intrathecal baclofen delivery systems and ventriculoperitoneal shunting systems: clinical series discussion. Pediatr Neurosurg [Epub ahead of print]

Agmo A, Paredes R (1985) GABAergic drugs and sexual behavior in the male rat. Eur J Pharmacol 112:371–378

Albright AL (1996a) Baclofen in the treatment of cerebral palsy. J Child Neurol 11:77–83

Albright AL (1996b) Intrathecal baclofen in cerebral palsy movement disorders. J Child Neurol 11(Suppl 1): S29–S35

Albright AL, Cervi A, Singletary J (1991) Intrathecal baclofen for spasticity in cerebral palsy. JAMA 265:1418–1422

Albright AL, Barry MJ, Fasick P, Barron W, Shultz B (1996) Continuous intrathecal baclofen infusion for symptomatic generalized dystonia. Neurosurgery 38:934–938; discussion 938–939

Almeida GL, Campbell SK, Girolami GL, Penn RD, Corcos DM (1997) Multidimensional assessment of motor function in a child with cerebral palsy following intrathecal administration of baclofen. Phys Ther 77:751–764

Armstrong RW, Steinbok P, Cochrane DD, Kube SD, Fife SE, Farrell K (1997) Intrathecally administered baclofen for treatment of children with spasticity of cerebral origin. J Neurosurg 87:409–414

Bayham IA, Sees JP, Nishnianidze T, Rogers KJ, Miller F (2016) Infection as a complication of intrathecal baclofen treatment in children with cerebral palsy. J Pediatr Orthop 36:305–309

Bennett MI, Tai YM, Symonds JM (1994) Staphylococcal meningitis following synchromed intrathecal pump implant: a case report. Pain 56:243–244

Boster A, Bennett S, Bilsky G, Gudesblatt M, Koelbel S, McManus M, Saulino M (2016) Best practices for intrathecal baclofen therapy: screening test. Neuromodulation 19:616–622

De Lissovoy G, Matza L, Green H, Werner M, Edgar T (2007) Cost-effectiveness of intrathecal baclofen therapy for the treatment of severe spasticity associated with cerebral palsy. J Child Neurol 22:49–59

Denys P, Mane M, Azouvi P, Chartier-Kastler E, Thiebaut JB, Bussel B (1998) Side effects of chronic intrathecal baclofen on erection and ejaculation in patients with spinal cord lesions. Arch Phys Med Rehabil 79:494–496

Erickson DL, Blacklock JB, Michaelson M, Sperling KB, Lo JN (1985) Control of spasticity by implantable continuous flow morphine pump. Neurosurgery 16:215–217

Gerszten PC, Albright AL, Barry MJ (1997) Effect on ambulation of continuous intrathecal baclofen infusion. Pediatr Neurosurg 27:40–44

Kita M, Goodkin DE (2000) Drugs used to treat spasticity. Drugs 59:487–495

Kraus T, Gegenleitner K, Svehlik M, Novak M, Steinwender G, Singer G (2017) Long-term therapy with intrathecal baclofen improves quality of life in children with severe spastic cerebral palsy. Eur J Paediatr Neurol 21:565–569

Leipheimer RE, Sachs BD (1988) GABAergic regulation of penile reflexes and copulation in rats. Physiol Behav 42:351–357

McLaughlin JF, Bjornson KF, Astley SJ et al (1998) Selective dorsal rhizotomy: efficacy and safety in an investigator-masked randomized clinical trial. Dev Med Child Neurol 40:220–232

Pruszczynski B, Sees J, Hulbert R, Church C, Henley J, Niiler T, Miller F (2017) The effect of continuous intrathecal baclofen therapy on ambulatory children with cerebral palsy. J Pediatr Orthop B [Epub ahead of print]

Rode G, Mertens P, Beneton C, Schmitt M, Boisson D (1999) Regression of vasomotor disorders under intrathecal baclofen in a case of spastic paraplegia. Spinal Cord 37:370–372

Saulino M, Guillemette S, Leier J, Hinnenthal J (2015) Medical cost impact in intrathecal baclofen therapy for severe spasticity. Neuromodulation 18:141–149

Saulino M, Anderson D, Doble J, Farid R, Gul F, Konrad P, Boster A (2016) Best practices for intrathecal baclofen therapy: troubleshooting. Neuromodulation 19:632–641

Steinbok P, Reiner AM, Beauchamp R, Armstrong RW, Cochrane DD, Kestle J (1997) A randomized clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic diplegic cerebral palsy [published erratum appears in Dev Med Child Neurol 1997;39(11): inside back cover]. Dev Med Child Neurol 39:178–84

Sweet CS, Wenger HC, Gross DM (1979) Central antihypertensive properties of muscimol and related gamma-aminobutyric acid agonists and the interaction of muscimol with baroreceptor reflexes. Can J Physiol Pharmacol 57:600–605

Wiens HD (1998) Spasticity in children with cerebral palsy: a retrospective review of the effects of intrathecal baclofen. Issues Compr Pediatr Nurs 21:49–61

Zierski J, Muller H, Dralle D, Wurdinger T (1988) Implanted pump systems for treatment of spasticity. Acta Neurochir Suppl 43:94–99